DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

9/30/03

San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502-7070
Telephone: 510/337-6700

Via Federal Express

Our Reference: 2925153

September 17, 2003

Carey E. Bolden
President
HDC Corporation
628 Gibraltar Court
Milpitas, CA 95035

WARNING LETTER

Dear Mr. Bolden:

During an inspection by the Food and Drug Administration (FDA) of your firm located in Milpitas, California, on April 14 to May 1, 2003, an investigator collected information that revealed serious regulatory problems involving the manufacture of your V-Cath Peripherally Inserted Central Catheter (PICC). These products are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformance with the Quality System (QS) regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations include, but are not limited to the following:

1. Failure to ensure that quality system requirements are effectively established and maintained at all levels of the organization as required in 21 CFR 820.20. For example, you have not ensured that written procedures are being followed in validating your device designs; design changes are validated, documented, and reviewed prior to implementation; and corrective and preventive actions are identified to prevent the recurrence of nonconforming product(s) and other quality problem(s).

   Your May 15, 2003, response to the form FDA-483 presented to your firm at the end of the inspection is not adequate in that you have failed to provide detailed information as to your corrective and preventive action to ensure that quality system requirements are effectively implemented throughout your organization. Please provide a detailed explanation in how your firm will ensure the implementation of your internal procedures and that they comply with the Quality System Regulation.

2. Failure to ensure written procedures are followed in validating and/or verifying design changes prior to their implementation as required in 21 CFR 820.30(i). For example, Engineering Change Order (ECO) 2002-006 was initiated to qualify a new vendor, to add [redacted] interval markings, and to change the [redacted] ingredient content from [redacted] to [redacted] to increase the strength of the new [redacted]. You implemented this ECO without: (A) Providing a rationale for the selected predetermined specifications used in the [redacted] (B) Following a valid statistical rationale or methods in the [redacted] and (C) Demonstrating that the [redacted] sized [redacted] containing [redacted] is equal to or better than the original catheter that contained [redacted]

   Your May 15, 2003, response is not adequate in that your corrective action plan is to review and research the raw data to obtain information that should have been identified and documented in the design history file. Further, your action plan does not address employee practices in preventing the recurrence of not formally documenting design changes.

3. Failure to review and approve all documents prior to their issuance as required in 21 CFR 820.40(a). For example, Engineering Change Order (ECO) 98-008 was issued on December 23, 1998 to change the [redacted] in the manufacturing of the [redacted] This change was transferred into production in 1999. The formal review and approval of this ECO did not occur until April 24, 2003.

   Your May 15, 2003, response to this observation is not adequate. The Design Control requirements of the Quality System became effective on June 1, 1997. The agency provided a one year grace period, between June 1, 1997 and June 1, 1998, during which time deviations from the requirement would not be noted on FDA-483s. Manufacturers were expected to be in compliance by June 1, 1998. As noted during our inspection, ECO 98-008 was developed/issued on December 23, 1998. Your response failed to address the actions needed to correct and prevent the recurrence of the noted observation.

4. Failure to perform design validation under defined operating conditions on initial production units, lots, or batches, or their equivalents as required in 21 CFR 820.30(g). In addition, design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions. Further, the results of the design validation, including identification of the design, methods, the date, and the individuals performing the validation shall be documented in the Design History File. ECO 98-008 was generated on December 23, 1998 to change the [redacted] content from [redacted] in the manufacturing of the [redacted] for its [redacted] catheters. This change was transferred into production in 1999 without formal review and approval of the design change. There is no documented evidence that this change had undergone design validation. However, management formally approved this

change on April 24, 2003 by signing ECO 98-008, even without evidence that a complete design validation study was performed.

Your May 15, 2003, response is not adequate. As noted by our investigator during the May 2003 inspection, there was no documented evidence that testing of production units were performed under actual or simulated use conditions. There was no evidence that management had reviewed and/or approved the changes prior to Mr. [redacted] signing the ECO on April 24, 2003. The change in the [redacted] amount from [redacted] was transferred and implemented into production in 1999. Your response failed to address the actions needed to correct and prevent the recurrence of this observation.

5. Failure to identify the actions needed to correct and prevent recurrence of nonconforming product and other quality problems as required in 21 CFR 820.100(a)(3). For example:

   A) Corrective Action Request (CAR) #138 was issued on January 4, 2002 to address the ". . . incidence rates related to breaks and leaks." The root cause was identified as "Users not following IFU" (Instructions for Use). The corrective actions taken were to analyze complaint data, to locate an alternate vendor, and to assess a new tubing supplier. Based on these proposed actions, the CAR was closed on April 5, 2002. However, the corrective and preventive action did not address the root cause, which was that the IFU was not being followed. Further, the alternate vendor was still being assessed when the CAR was closed, therefore the issues related to the breaks and leaks were not fully addressed.

   B) On February 11, 2002, CAR #141 was issued due to high quarterly readings of bioburden count per packaged unit (a unit consists of an IFU, a patient information booklet, and the medical device). The mean total CFU/PU was [redacted] which exceeded the limit of [redacted] CFU/PU as identified by your bioburden Testing Procedure, #QCP-128, Rev. #3. An investigation was performed and your firm identified that the paper components were the highest contributing source of the bioburden. Your corrective action was to discontinue the monitoring of bioburden levels being caused by the paper components. This CAR was closed on June 10, 2002 without identifying and/or controlling the source of the bio and/or non-bio particulates.

   C) On April 4, 2002, CAR #147 was issued based on complaints that the needles, a catheter component, were blocked/occluded with white material. You submitted a petition to your vendor, [redacted], on April 12, 2002 to investigate the source of nonconformity. As of the date of our inspection, your vendor had not responded to your petition, and on April 30, 2002, the CAR was closed without the performance of an investigation to determine the root cause to correct and prevent this nonconformity.

   Your May 15, 2003, response to observations 6 and 7 of the FDA-483 is not adequate in that you failed to address the actions needed to correct and prevent the

recurrence of the observations. Your response notes that you will re-visit the Corrective Action Request reports we identified as being inadequate during the May 2003 inspection. It is your responsibility to ensure that your Quality System properly identifies and addresses all quality deviations in your subsystems.

In addition to the deviations described above that render your device adulterated, our inspection revealed that your device is also misbranded within the meaning of section 502(t)(2) of the Act, in that your firm failed or refused to furnish material or information required by or under section 519 of the Act and the Medical Device Reporting (MDR) regulations at 21 CFR Part 803. The MDR regulations require device manufacturers to report, within 30 days of receiving or otherwise becoming aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer: (1) may have caused or contributed to a death or serious injury; or (2) has malfunctioned and such device or a similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur. [21 CFR 803.50(a)] Your firm failed to submit MDR reports as required in the following instances:

1. The information contained in complaint #1573 reasonably suggests that your device may have caused or contributed to a serious injury to the patient that necessitated medical intervention to preclude permanent impairment of a body function or permanent damage to a body structure, in order to remove the broken piece of the V-Cath PICC. A femoral venous access had to be performed by the physician to snare the remaining tubing after the V-Cath PICC catheter broke during removal from the patient.

2. The information contained in complaints #1707, #1582, and #1562 reasonably suggests that your device may have caused or contributed to a serious injury that necessitated medical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. In all three complaints, the patients were transported to the hospital or appeared in the ER for removal of the broken PICC lines. In complaint #1582, the second patient appeared in the ER because their PICC line fell out. Attempts to remove it resulted in fracture of the tubing. In all of these complaints, the information reasonably suggests that medical intervention was necessary to remove the broken V-Cath PICC catheters from the patient's arm.

A serious injury is defined as an injury or illness that: (1) is life-threatening; (2) results in permanent impairment of a body function or permanent damage to body structure; or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. [21 CFR 820.3(bb)(1)]. This definition is being provided to you so that your firm can correctly identify your MDR reports. Review of the CDRH databases disclosed that HDC Corporation submitted 23 reports for the V-Cath PICC during the last year, and that 5 were classified as "serious injuries," while the remaining 18 were identified as "other" reports. It is important to note that almost all of the 18 "other" reports mentioned the necessity for medical or

surgical intervention. Please make sure that the above definition is added to your MDR procedures, and that it be considered when classifying future MDR reports.

Your May 15, 2003, response to this observation is not adequate as your letter implies that you will only review those specific complaints listed on the FDA-483. It is your responsibility to assure that any and all complaints received are reviewed and investigated, and where necessary, that MDR reports are filed. Further, you have failed to address employee training activities that will prevent the recurrence of the noted observation.

This letter is not intended to be an all-inclusive list of violations. It is your responsibility to ensure that all requirements of the Act are being met. The specific violations noted in this letter and in the form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be system problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates of Product for Export will be approved until all violations relating to the subject device has been corrected.

You should take prompt actions to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or the imposition of civil penalties.

You should notify our office in writing, within fifteen (15) working days of your receipt of this letter, of the specific steps you have taken or will take to correct these violations and preclude their recurrence. If corrective action cannot be completed within fifteen working days, state the reason for the delay and the time frame within which corrections will be completed. Your response should address each deficiency brought to your attention during the inspection and in this letter, and should include copies of any documentation demonstrating that corrections have been made. Please direct your reply to Lawton W. Lum, Compliance Officer, United States Food and Drug Administration, 1431 Harbor Bay Parkway, Alameda, CA 94502.

Sincerely yours,

Dennis K. Linsley
District Director
San Francisco District